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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,084	08/09/2001	Gil Tenne	U 013591-0	4110

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 02/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,084	TENNE ET AL.	
	Examiner	Art Unit	
	Ja-Na A Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *1-15 and 36-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the invention of group I has some of the same steps as the invention of group II, therefore the groups should be rejoined. This is not found persuasive because inventions in group I and II are different methods. The methods are distinct because the method of Group II has different effects as compared to group I. Further group II requires an isolation step; preparation step; and interaction step that group I does not. In view of the different steps, it is clear that the inventions are unrelated. Therefore, requirement is still deemed proper and is therefore made FINAL.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 16-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for an early diagnosis of cancer in a subject comprising a provision step; treatment step; identification step; determination of *E.coli, S. bovis* and/or *Enterococcus* species step; isolation of *E.coli, S. bovis* and/or *Enterococcus* species step; preparation step; and interaction step, does not reasonably provide enablement for a method for an early diagnosis of cancer in a subject comprising a provision step; treatment step; identification step; determination of any microorganism step; isolation of any microorganism step; preparation step; and interaction step. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification teaches that healthy people show a higher percentage of *E.coli* with cancerolytic activity as compared to cancer patients (page 2 lines 24-27). Example 1 teaches the preparation of *E.coli, S.bovis* and *Enterococcus* species to be used within the method (page 12). The results on page 13 show the presence of *Enterococcus* and *S. bovis* species. There is no teaching of the broad class microorganisms. Microorganisms include bacteria (eubacteria, archaebacteria), fungi (yeasts, molds), protozoa, microscopic algae, viruses, various parasitic worms. The specification fails to teach examples of any type of microorganism that can be used in the method to aid the determination of an early cancer diagnosis in the manner instantly claimed. There are

no examples teaching how to make and use the method with out the specific bacteria. Moreover, there are no steps which teach how the determination, isolation and preparation of a parasite will determine the early diagnosis of cancer. Therefore, the specification fails to enable a method for an early diagnosis of cancer in a subject comprising a provision step; treatment step; identification step; determination of any microorganism step; isolation of any microorganism step; preparation step; and interaction step.

Applicants' have provided no guidance to enable one of ordinary skill in the art as to how determine, without undue experimentation, every microorganism useable in the method; therefore, one of skill in the art would have to locate de novo steps required for a method for an early diagnosis of cancer in a subject. Given the lack of guidance contained in the specification and the unpredictability for early cancer diagnosis, one of skill in the art could not make or use the broadly claimed invention without undue experimentation. The specification fails to provide an enabling disclosure for a method for an early diagnosis of cancer in a subject comprising a provision step; treatment step; identification step; determination of any microorganism step; isolation of any microorganism step; preparation step; and interaction step as recited in the claims. There is no requirement or limitation for using only the specifically recited bacterial species. In view of the lack of guidance contained in the specification and the unpredictability for the early diagnosis of cancer, one skilled in the art could not make or use the broadly claimed invention without undue experimentation.

4. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification lacks complete deposit information for the deposit of cells having the Accession NO. ATCC MCF7. Because it is not clear that cell lines possessing the properties of Accession NO. ATCC MCF7 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of Accession NO. ATCC MCF7, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to

recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;

3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cancer cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

5. Claims 16-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of the claims ~~are drawn to~~ recite a method for an early diagnosis of cancer in a subject, however there are no steps within the method which teach how to determine whether there has been an early diagnosis of cancer. The claims lack a positive recitation of method steps that recite how to diagnose cancer. For instance

there is no step that correlates the determination of the tumor cell necrosis index to the early diagnosis of cancer. Therefore, the goal of the preamble is not commensurate with the steps of the method.

The term "early diagnosis" in the claims is a relative term which renders the claim indefinite. The term "early diagnosis" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the term cannot be ascertained, for instance, how early must cancer be diagnosed; or what is early in reference too? Therefore, the term is vague and clarification is required to overcome the rejection.

6. Claim 12 recites the limitation "a corresponding sample" in the claim. There is insufficient antecedent basis for this limitation in the claim. It is unclear what the corresponding sample is; i.e., whether it is a duplicate sample or a control sample. It is unclear where the corresponding sample came from. Therefore the claim is rejected.

7. Claim 18 recites the removal of undesirable contamination. The term "undesirable contamination" in the claims is a relative term that renders the claim indefinite. What makes something undesirable? What attributes must the component possess to be deemed undesirable? The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the

invention. The metes and bounds of the term cannot be ascertained and clarification is required to overcome the rejection.

8. Claim 32 recites the ruses of a standard culture of cancer cells. The term in the claims is a relative term that renders the claim indefinite. What makes the cancer cells standard? What attributes must the cancer cells possess to be deemed standard? The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the term cannot be ascertained and clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 16—32 and 34-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Karapetian (US Patent 5,344,762). Karapetian teaches a method for the early diagnosis of cancer. The present invention provides a method of early diagnosis in a human, wherein human feces-derived sample of bacteria selected from *E.coli* and *S. faecalis* is subjected to incubation with a standard culture of cancer cells for a period of time sufficient to enable the interaction between the bacteria and the cancer cells and

effecting the determination (col. 1 lines 59-68). The determination is calculated by calculating the Tumor Cell Necrosis Index (TCNI) using the recited formula. It is noted that the TCNI formula is the same formula recited in the instant application. A healthy patient will have *E.coli* and *S. faecalis* with a relatively high TCNI value ~~will~~ while a less healthy patient will have a lower TCNI value (col. 2 lines 26-40). The bacteria ~~has~~ have been treated, identified, isolated and cultured on Endo agar medium, incubated with cancer cells and thereafter the TCNI was calculated (col. 5 lines 9-33). See example 1. The method is simple, accurate and readily adaptable to mass screening techniques (col. 6 lines 59-64).

Therefore, Karapetian teaches a method of early diagnosis of cancer comprising the same steps as those recited by the instant claims.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines

February 4, 2003

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
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